

Practitioner's Docket No. MPI98-148PIUSRCE2M

U.S.S.N. 09/673,302

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. – 78. (Canceled)

79. (Previously Presented) A transgenic mouse which expresses a transgene integrated into its genome, wherein the transgene comprises DNA encoding a mutant GP IIIa (β_3) protein having two conservative amino acid substitutions for two wild type tyrosine residues in its mutant cytoplasmic domain, wherein said transgenic mouse has platelets with reduced or absent phosphorylation of said mutant GP IIIa (β_3) protein compared to platelets with wild type GP IIIa (β_3) protein from a wild type mouse.

80. (Previously Presented) The transgenic mouse of claim 79 wherein the mutant cytoplasmic domain comprises conservative amino acid substitutions for the wild type tyrosine residues depicted in the cytoplasmic domain sequence for GP IIIa in Figure 2 (SEQ ID NO:1).

81. (Previously Presented) The transgenic mouse of claim 79 wherein each cytoplasmic wild type tyrosine residue is substituted by a mutant phenylalanine residue.

82. (Canceled)

83. (Currently Amended) A method of preparing a transgenic mouse heterozygous for a mutant GP IIIa (β_3) gene, wherein the mutant gene encodes a mutant GP IIIa (β_3) protein

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having a two conservative amino acid ~~substitution~~ substitutions for a two wild type tyrosine residues in its mutant cytoplasmic domain, the method comprising:

- a) introducing into embryonic stem cells a nucleic acid molecule comprising the mutant GP IIIa (β_3) gene, wherein the mutant gene encodes the mutant GP IIIa (β_3) protein;
- b) injecting transformed cells from step a) into one or more blastocysts; and
- c) generating a chimeric mouse from the blastocysts of step b);
- d) mating the chimeric mouse of step c) with a wild type mouse to obtain a transgenic mouse heterozygous for a mutant GP IIIa (β_3) gene,

wherein said transgenic mouse has platelets with reduced or absent phosphorylation of said mutant GP IIIa (β_3) protein compared to platelets with wild type GP IIIa (β_3) protein from a wild type mouse.

84. (Currently Amended) The method of claim 83 wherein the mutant cytoplasmic domain comprises a conservative amino acid ~~substitution~~ substitutions for a the wild type tyrosine ~~residue~~ residues depicted in the cytoplasmic domain sequence for GP IIIa in Figure 2 (SEQ ID NO:1).

85. (Currently Amended) The method of claim 83 wherein ~~the~~ each conservative amino acid substitute in the mutant cytoplasmic domain is phenylalanine.

86. (Previously Presented) The method of claim 83 further comprising:

- e) mating the transgenic mouse; and
- f) selecting a mouse homozygous for the mutant GP IIIa (β_3) gene.

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87. (Currently Amended) A method of preparing a transgenic mouse heterozygous for a mutant GP IIIa (β_3) gene encoding a mutant GP IIIa (β_3) protein having a two conservative amino acid ~~substitution~~ substitutions for a two wild type tyrosine residues in its mutant cytoplasmic domain, the method comprising:
- a) introducing into embryonic stem cells a nucleic acid molecule comprising the mutant GP IIIa (β_3) gene encoding the mutant GP IIIa (β_3) protein and a selectable marker flanked by FRT sites, to produce one or more transformed embryonic stem cells;
 - b) identifying and selecting the transformed cells;
 - c) removing the selectable marker from the transformed cells selected in step b) by transient transformation with FLP recombinase;
 - d) injecting transformed cells from step c) into one or more blastocysts; and
 - e) generating a transgenic mouse from the blastocysts of step d), wherein the transgenic mouse comprising the mutant GP IIIa gene is heterozygous for the mutant GP IIIa gene,
- wherein said transgenic mouse has platelets with reduced or absent phosphorylation of said mutant GP IIIa (β_3) protein compared to platelets with wild type GP IIIa (β_3) protein from a wild type mouse.
88. (Currently Amended) The method of claim 87 wherein the each conservative amino acid substitute in the mutant cytoplasmic domain is phenylalanine.

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89. (Currently Amended) The method of claim 87 wherein the mutant cytoplasmic domain comprises a conservative amino acid ~~substitution~~ substitutions for a the wild type tyrosine ~~residue~~ residues depicted in the cytoplasmic domain sequence for GP IIIa in Figure 2 (SEQ ID NO:1).
90. (Previously Presented) The method of claim 87 further comprising:
- f) mating the transgenic mouse; and
 - g) selecting a transgenic mouse homozygous for the mutant GP IIIa (β_3) gene.
91. - 92. (Canceled)
93. (Currently Amended) A method of determining the effect of an agent on a biological response of the transgenic mouse of claim ~~76~~ 79, wherein the biological response is mediated by GP IIIa (β_3) phosphorylation, the method comprising:
- a). administering the agent to the mouse;
 - b). determining the effect of the agent on the biological response mediated by GP IIIa (β_3) phosphorylation.
94. (Previously Presented) The transgenic mouse of claim 79, wherein the DNA encoding the mutant GPIIIa replaces the DNA encoding the wild type GP IIIa.
95. (Previously Presented) The transgenic mouse of claim 94, wherein replacement of the DNA encoding the wild type GP IIIa results in a transgenic mouse which is heterozygous for the DNA encoding the mutant GP IIIa gene.

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96. (Previously Presented) The transgenic mouse of claim 94, wherein replacement of the DNA encoding the wild type GP IIIa results in a transgenic mouse which is homozygous for the DNA encoding the mutant GP IIIa gene.
97. (Previously Presented) Platelets isolated from blood plasma of the transgenic mouse of claim 79.
98. (Previously Presented) Platelets isolated from blood plasma of the transgenic mouse of claim 96.
99. (Currently Amended) A method of determining the effect of an agent on a biological response of the transgenic mouse of claim ~~79~~ 96, wherein the biological response is mediated by GP IIIa (β_3) phosphorylation, the method comprising:
- a). administering the agent to the mouse;
 - b). determining the effect of the agent on the biological response mediated by GP IIIa (β_3) phosphorylation.

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